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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/977,155
Filing Date: October 12, 2001
Appellant(s): HERZ ET AL.

Richard Aron Osman (Reg. No.36,627)
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 16, 2005 appealing from the Office action mailed May 18, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct. The appeal involves claims 1-20.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

A. Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994).

B. Herz (Neuron, Vol29, pages 571-581).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

A. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1-9 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994).

Willnow et al. teach methods involving LRP-mini receptors . See abstract. The LRP-mini receptor comprises 11 complement-type repeats (LDL receptor ligand – polypeptide) and one EGF precursor homologous domain (region IV) is fused to the carboxyl-terminal segment of LRP (six EGF repeats, transmembrane segment, and the cytoplasmic tail). See page 5828, 2nd column, 1ts paragraph, and figure 1.

Region IV contains a proteolytic site, which allows for protease digestion into a 80kDa amino-terminal and a 85kDa carboxyl-terminal fragment (C-terminal tail). The LRP regions were prepared via SDS gel electrophoresis and transferred to nitrocellulose (solid-phase affinity adsorption). Polyclonal anti-LRP antibodies directed against the cytoplasmic tail of LRP and ^{125}I goat anti-rabbit IgG (affinity tag) were utilized in Western blotting procedures to detect the mini receptors membrane extracts from the cell lines. Bottom of page 15828 to 15829 and figure 2.

Claim Rejections - 35 USC § 103

B. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994) in view of Herz (Neuron, Vol29, pages 571-581).

Please see Willnow et al. as set forth above.

Willnow et al. differs from the instant invention in not teaching all the possible LDL receptor (namely LRP, LRP1b, megalin, LDLR, VLDLR,ApoER2, MEGF7, LRP5, LRP6, and LR11).

However, Herz discloses the core members of the LDL receptor gene. See abstract and figure 1. Herz further teaches each LDL possible role and involvement in cellular events. See Table 1. The core members of the LDL receptor gene family include the LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7. See page 571, 1st column, 2nd paragraph. Herz et al. disclose that these seven core members of the LDL receptor gene family are "structurally closely related cell surface receptor".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use various known LDL receptor equivalents having similar structures and found native to the membrane as taught by Herz in the method of Willnow et al. because Herz taught that the LDL receptor gene family consists of seven structurally related cell surface receptors (LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7). See abstract. Therefore the analysis of any of the known equivalent receptors taught by Herz in the method of Willnow et al. would have been obvious because the receptors would perform the same function in the same manner as the receptors found in Willnow et al.

In other words the behavior of one compound predicts the behavior of equivalents absent evidence to the contrary. Further, applicant has not set forth reasons for the utility of any particular receptor.

Accordingly, obviousness is based on the similarity of structure, function, and similar properties. In re Payne, 606 F.2d 303, 203, USPQ 245, 254-55 (CCPA 1979).

Allowable Subject Matter

C. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

(10) Response to Arguments

Applicant contends that Willnow et al. describes truncated LRPs comprising subsets of the native N-terminal domains. Therefore the proteolytic process does not occur at intramembraneous or cytoplasmic sites to liberate a cytoplasmic tail. This argument was carefully considered but not found persuasive because Willnow et al. disclose LRPs subsets that include the cytoplasmic tail as well as the detection of the cytoplasmic tail. For example on page 15828, 2nd column, middle section and figure 1 - regions II and IV are fused to the membrane (carboxyl-terminal segment) and the cytoplasmic tail (cytoplasmic segments of LRP).

Applicant also contends that the instant invention discloses LRP and other members of the LDL receptor gene family that undergo distinct endoproteolytic processing events resulting in the release of their cytoplasmic tails into the cytoplasm, while the prior art liberates an extracellular domain wherein the proteolysis process in the prior art does not *occur at intramembraneous or cytoplasmic sites*. This argument was carefully considered but not found persuasive because the claims do not recite these limitations. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a cytoplasmic tail released at intramembraneous or cytoplasmic sites) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims merely require a protease that cleaves the domain and releases the tail. There are various domains located in the polypeptide of claim 1 step (a). This is supported in the arguments set forth by Applicant in the appeal brief filed 9/16/05 on page 2 – 3rd paragraph wherein it states "the tail may comprise the native cytoplasmic domain of the LDL receptor or a truncation thereof". Therefore, it is clear that the recitation of a protease cleavage at a domain does not necessarily result in the cleavage of a cytoplasmic tail, free from any additional membrane components. As applicant have argued.

Applicant argues that the protease taught by Willnow cleaves at the N-terminal yielding a membrane-bound fragment (cytoplasmic tail comprising membrane components). This membrane bound fragment is subsequently bio-chemically extracted to release the C-terminal product. Therefore, Willnow is different from the claimed invention because the instant claims do not require a biochemical extraction step. This argument was carefully considered but not found persuasive because the claims utilizes comprises which is "open language" allowing for the inclusion of steps not recited by the claims.

In Willnow et al., proteolytic processing resulting in a separation of the LRP within a domain to produce a N-terminal and C-terminal product is seen on page 15829 1st column. In one embodiment, the cytoplasmic tail of LRP is detected with polyclonal anti-LRP antibodies by Western blotting. See page 15828 2nd column 2nd paragraph. On page 15829, 1st column, 1st paragraph – Region IV is taught to be cleaved by intracellular proteases that cleave LRP at a tetrabasic site in the eighth EGF precursor domain and these proteases can process LRP into a 80kDa amino terminal and a 85kDa carboxyl-terminal fragment (lanes 2 and 4 of figure 2A). Accordingly, Willnow et al. teach proteolysis procedures that produce a N-terminal and C-terminal of a LDL receptor domain fused to a c-terminal tails and well as c-terminal tail detection.

In the supplemental response faxed 3/9/05, Applicants contend that Willnow et al. describe LRP cleavage at an N-terminal and no theoretical concept or experimental data is disclosed to suggest the release of the C-terminal tail from the membrane.

This argument has been carefully considered but not found persuasive because Willnow et al. teach C-terminal tail liberation and detection. See page 15828 2nd column through page 15829 1st column. Further, a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

Applicants argue that Willnow et al. do not teach protease liberation of the c-terminal tail of LDR, therefore the combination of Willnow et al. and Herz et al. cannot make the invention obvious. This argument has been carefully considered but is not found persuasive. The arguments against Willnow et al. have been addressed a priori and were not found persuasive, therefore the rejection of Willnow et al. in view of Herz et al. is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

4/17/06

Lisa V. Daniels-CooK

December 7, 2005

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